

## REMARKS

With reference to the Official Action, the paragraph on page 2 with respect to priority is duly noted, but it does not have any application to the present case.

The reference to the Specification is duly noted and correction has been made to include in the Specification two paragraphs and a title directed to a Brief Description of the Drawings. This material was inserted on page 2 of the substitute specification and care was taken not to include any new matter.

With reference to the claim rejections under 35 USC 112, it is respectfully noted that the subject matter objected to was disclosed in the application in claim 25, and since it was in a claim, there is no question that the applicant intended that it be part of his invention. This claim 25 has been amended to clarify what the applicant contends is his invention and to reasonably convey to one skilled in the art that at the time the inventor filed the application, he had possession of the invention as recited in the claim 25. More particularly, resort was had to the Internet and attached hereto are web pages from three of a multitude of sites, discussing oxygen therapy. Oxygen therapy is notoriously old and well known by anyone of ordinary skill in the art to which this application pertains. The three web pages, (1) <http://www.mtsinai.org> (discusses "What is Oxygen Therapy?" gives a general overview); (2) <http://www.oxytherapy.com> (discusses oxygen therapies in veterinary medicine, and notes that it is not new); and (3) <http://ahcpr.gov> (discusses Hyperbaric Oxygen Therapy for Brain Injury, Cerebral Palsy, and Stroke, and the general application of the therapy). These three web pages are a good indication that the oxygen therapies are well known to those of skill in this art. With claim 25 being amended to particularly point out and distinctly claim applicant's invention in this regard, it is respectfully solicited that the objection to claim 25 concerning sec. 112, in good conscience, be withdrawn.

With reference to the rejection of claims 12, 13, 15, 19 and 20 under 35 USC 102(b) as being clearly [sic] by Reiss et al, it is respectfully pointed out that claim 12, the independent claim of the group listed above, claims a gel having a polyaphron structure and Reiss et al gels **DO NOT**. Of particular interest is the IPER issued by the International Bureau during the PCT process, which specifically reported that the invention was novel and inventive. See translation of relevant portion of the IPER quoted below, copy of translation attached:

Reference is made to the following document:  
D1: US-A-5, 573,573.

3. Claims 1-11 meet the requirements of PCT Article 33(2) and (3) because their subject matter is novel and inventive (see below).

### 3.1 Novelty:

A gel having a polyaphron structure and containing a fluorocarbon, water, and at least one fluorosurfactant of the general formula as per Claim1 is not contained in the prior art cited in the search report.

### 3.2 Inventive step

The problem addressed by the present application was to provide a plastically formable implant that also allows long-term use.

As suggested in Claim 1 and supported by the examples of the application, this problem is solved by an implant in the form of a fluoro-containing gel, the gel having a polyaphron structure and containing, in addition to the fluorocarbon, water and at least one fluorosurfactant of the general formula according to Claim 1.

Document D1, which is regarded as the closest prior art, discloses (see Claims 1 and 45 in combination with column 3, lines 14-22, for example) fluorocontaining gels, for topically treating the skin, having a polyaphron and containing, in addition to the fluorocarbon, water and a fluorosurfactant that is an amineoxide.

Amineoxide fluorosurfactants do not fall within the scope of the general formula according to Claim 1. Furthermore, as demonstrated in the present application (see page 2, second paragraph), it is known that gels as per Claim 1 are irreparably damaged or dissolved when subjected to heating or mechanical pressure.

In the light of D1, it was in no way obvious to a person skilled in the art that the implant claimed in Claim 1 would solve the problem of long-term use.

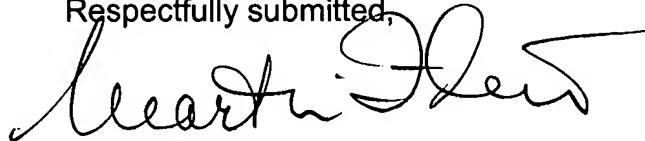
As noted during the introductory part of the present application, gels according to Reiss et al are irreversibly destroyed upon heating or by applying mechanical pressure. For the reasons given above and because the claimed invention as recited in claim 12 would not be obvious to a person skilled in the art, it is earnestly solicited that claim 12 be favorably reconsidered and considered allowable. By the same token, the dependent claims that depend from claim 12 directly or indirectly, should also be considered as allowable since they contain all the limitations of allowable claim 12.

With respect to claims 14, 16-18, and 21-24 that were objected to as depending from a rejected claim, but would have been otherwise allowable, these claims have been restated as follows, incorporating all the limitations of the claims from which they depended. Claim 14 has been rewritten as claim 26; claim 16 has been rewritten as claim 27; claim 18 has been rewritten as claim 28; claim 21 has been rewritten as claim 29; claim 22 has been rewritten as claim 30 and claim 24 has been rewritten as claim 31. In addition, claim 17 has been made dependent on allowable claim 27; and claim 23 has been made dependent on allowable claim 30. Also, seven method claims 31 to 37 have been added directed to the methods of using the implants of claim 12 and claims 26 to 31. Claim 31 is allowable for the reasons expressed with respect to claim 12. Claims 32 to 37 are based on allowable implants, and accordingly, are in themselves allowable.

In light of the foregoing remarks, this application should be in condition for allowance, and early passage of this case to issue is respectfully requested. If there are any questions regarding this amendment or the application in general, a telephone call to the undersigned would be appreciated since this should expedite the prosecution of the application for all concerned.

Please charge any required fee (or credit any overpayments of fees) to the Deposit Account of the undersigned, Account No. 500601 (Docket no. 754-X01-003).

Respectfully submitted,



Martin Fleit, Reg. #16,900

**Enclosures:** Petition for Extension of Time

Web pages (3)

Translation of IPER pages

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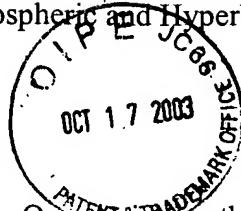


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(Signature of person mailing paper or fee)

MARTIN FLEIT

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## WHAT IS OXYGEN THERAPY?

Oxygen, of course, is part of the air we breathe. Oxygen is also the most widely prescribed "drug" in hospitals; about a quarter of all patients entering an acute care hospital will receive inhaled oxygen at some point in their stay. Since air already contains 21% oxygen, what doctors prescribe is more accurately known as *supplemental* oxygen, i.e., an inhaled oxygen concentration greater than the 21% in surrounding air. Sometimes the gas mixture prescribed is called "enriched" air, to distinguish it from "ordinary" air.

In hospitals, 100% oxygen is piped into each patient's room, ready for delivery at whatever concentration needed. The actual percentage of oxygen delivered is determined by the type of appliance used to bring the pure oxygen from the wall source to the patient's face, e.g., nasal prongs or various types of face mask. These appliances serve to mix the 100% oxygen from the wall source with the 21% oxygen from ordinary air; depending on the appliance used, the percentage of oxygen delivered to the patient can range between just above 21% to over 90%.

The oxygen percentage a doctor orders depends on the clinical condition of the patient. Generally, the lower the patient's oxygen level, the higher the O<sub>2</sub> concentration. Pure or undiluted (100%) oxygen is only used rarely, and then only in an intensive care unit. To minimize the risk of oxygen toxicity physicians try to keep the oxygen concentration at 40% or lower.



Oxygen Therapies (especially Ozone Therapy) in Veterinary Medicine is not new.

Animals have a lot of pathology which can be superimposed to human being diseases, moreover, there are no placebo effects in Veterinary Medicine.

This area has been created to encourage those using Oxygen Therapies in Veterinary Medicine to share information not only with each other, but everyone in the Oxygen Therapy community.

In 1997, Prof. Paolo Scrollavezza and his colleagues presented the paper Ozone Treatment and Blood Lactate Variation after Thoroughbred Racehorses. This paper was presented at the World Equine Veterinary Association Mondial Congress.

In 1997 in Havana, Cuba, Prof. Paolo Scrollavezza and his colleagues presented their research paper named Ozone Treatment in Mastitis, Metritis and Retention of Fetal Membranes in the Dairy Cow.

In July 2000, Japan researchers successfully used ozone therapy and documented their findings in the paper Intramammary application of ozone therapy to acute clinical mastitis in dairy cows.



Evidence Report/Technology Assessment: Number 85

# Hyperbaric Oxygen Therapy for Brain Injury, Cerebral Palsy, and Stroke

## Summary

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Under its Evidence-based Practice Program, the Agency for Healthcare Research and Quality (AHRQ) is developing scientific information for other agencies and organizations on which to base clinical guidelines, performance measures, and other quality improvement tools. Contractor institutions review all relevant scientific literature on assigned clinical care topics and produce evidence reports and technology assessments, conduct research on methodologies and the effectiveness of their implementation, and participate in technical assistance activities.

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## Overview

Hyperbaric oxygen therapy (HBOT) is the inhalation of 100 percent oxygen inside a hyperbaric chamber that is pressurized to greater than 1 atmosphere (atm). HBOT causes both mechanical and physiologic effects by inducing a state of increased pressure and hyperoxia. HBOT is typically administered at 1 to 3 atm. While the duration of an HBOT session is typically 90 to 120 minutes, the duration, frequency, and cumulative number of sessions have not been standardized.

HBOT is administered in two primary ways, using a monoplace chamber or a multiplace chamber. The monoplace chamber is the less-costly option for initial setup and operation but provides less opportunity for patient interaction while in the chamber. Multiplace chambers allow medical personnel to work in the chamber and care for acute patients to some extent. The entire multiplace chamber is pressurized, so medical personnel may require a controlled decompression, depending on how long they were exposed to the hyperbaric air environment.

The purpose of this report is to provide a guide to the strengths and limitations of the evidence about the use of HBOT to treat patients who have brain injury, cerebral palsy, and stroke. Brain injury can be caused by an external physical force (also known as traumatic brain injury, or TBI); rapid acceleration or deceleration of the head; bleeding within or around the brain; lack of sufficient oxygen to the brain; or toxic substances passing through the blood-brain barrier. Brain injury results in temporary or permanent impairment of cognitive, emotional, and/or physical functioning. Cerebral palsy refers to a motor deficit that usually manifests itself by 2

years of age and is secondary to an abnormality of at least the part of the brain that relates to motor function. Stroke refers to a sudden interruption of the blood supply to the brain, usually caused by a blocked artery or a ruptured blood vessel, leading to an interruption of homeostasis of cells, and symptoms such as loss of speech and loss of motor function.

While these conditions have different etiologies, prognostic factors, and outcomes, they also have important similarities. Each condition represents a broad spectrum, from barely perceptible or mild disabilities to devastating ones. All three are characterized by acute and chronic phases and by changes over time in the type and degree of disability. Another similarity is that the outcome of conventional treatment is often unsatisfactory. For brain injury in particular, there is a strong sense that conventional treatment has made little impact on outcomes.

Predicting the outcome of brain injury, cerebral palsy, and stroke is difficult. Prognostic instruments, such as the Glasgow Coma Scale (GCS) for brain injury, are not precise enough to reliably predict an individual patient's mortality and long-term functional status. Various prognostic criteria for the cerebral palsy patient's function have been developed over the years. For example, if a patient is not sitting independently when placed by age 2, then one can predict with approximately 95 percent confidence that he/she never will be able to walk. However, it is not possible to predict precisely when an individual patient is likely to acquire a particular ability, such as smiling, recognizing other individuals, or saying or understanding a new word.

Mortality and morbidity from a stroke are related to older age, history of myocardial infarction, cardiac arrhythmias, diabetes mellitus, and the number of stroke deficits. Functional recovery is dependent on numerous variables, including age, neurologic deficit, comorbidities, psychosocial factors, educational level, vocational status, and characteristics of the stroke survivor's environment.

The report focuses on the quality and consistency of studies reporting clinical outcomes of the use of HBOT in humans who have brain injury, cerebral palsy, or stroke. This information can be used to help providers counsel patients who use this therapy and to identify future research needs.

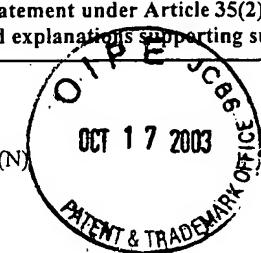
## INTERNATIONAL PRELIMINARY EXAMINATION REPORT

International application No.  
PCT/EP 00/05208

## V. Reasoned statement under Article 35(2) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

## 1. Statement

Novelty (N)



Inventive step (IS)

Industrial applicability (IA)

Claims

1-11

YES

Claims

NO

Claims

1-11

YES

Claims

NO

Claims

1-6, 7-11 (see attachment)

YES

Claims

NO

## 2. Citations and explanations

## 2. Reference is made to the following document:

D1: US-A-5 573 573.

3. Claims 1-11 meet the requirements of PCT Article 33(2) and (3) because their subject matter is novel and inventive (see below).

3.1 **Novelty:**

A gel having a polyaphron structure and containing a fluorocarbon, water, and at least one fluorosurfactant of the general formula as per Claim 1 is not contained in the prior art cited in the search report.

3.2 **Inventive step**

The problem addressed by the present application was to provide a plastically formable implant that also allows long-term use.

As suggested in Claim 1 and supported by the

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examples of the application, this problem is solved by an implant in the form of a fluoro-containing gel, the gel having a polyaphron structure and containing, in addition to the fluorocarbon, water and at least one fluorosurfactant of the general formula according to Claim 1.

Document D1, which is regarded as the closest prior art, discloses (see Claims 1 and 45 in combination with column 3, lines 14-22, for example) fluoro-containing gels, for topically treating the skin, having a polyaphron and containing, in addition to the fluorocarbon, water and a fluorosurfactant that is an amineoxide.

Amineoxide fluorosurfactants do not fall within the scope of the general formula according to Claim 1. Furthermore, as demonstrated in the present application (see page 2, second paragraph), it is known that gels as per Claim 1 are irreparably damaged or dissolved when subjected to heating or mechanical pressure.

In the light of D1, it was in no way obvious to a person skilled in the art that the implant claimed in Claim 1 would solve the problem of long-term use.

- 3.3 Claims 2-6 are dependent on Claim 1. Claims 7-11 pertain to the medical use of the implants as per the preceding claims. Thus, Claims 2-11 likewise meet the PCT requirements for novelty and inventive step.
4. Claims 1-6 meet the criterion of PCT Article 33(4) because their subject matter is industrially

**INTERNATIONAL PRELIMINARY EXAMINATION REPORT**

International application No.

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applicable.

5. The PCT does not contain uniform criteria for assessing the industrial applicability of the subject matter of Claims 7-11. Patentability may depend on the wording of the claims. The EPO, for example, does not recognise the industrial applicability of claims to the use of a compound in a medical treatment; it does, however, allow claims to the first use of a known compound in a medical treatment or the use of such a compound to manufacture a drug for a new medical treatment.